

**Amendments to the Specification:**

Please replace paragraph 0010 with the following paragraph:

Topiramate is an anticonvulsant intended for use as an antiepileptic drug. It is considered a broad spectrum anti-epileptic drug (AED) because it works to prevent both partial onset and generalized seizures. Epilepsy is a chronic condition characterized by recurrent, unprovoked seizures, or electrical disturbances in the brain that can alter a patient's consciousness, movement, or behaviors. Seizures are characterized as either partial or generalized, depending on where they originate in the brain. Epilepsy affects an estimated 2.3 million Americans and each year approximately 181,000 people in the United States are newly diagnosed with the condition. See <http://www.pharmaceuticalonline.com>.

Please replace paragraph 0013 with the following paragraph:

Patients newly diagnosed with epilepsy are routinely prescribed multiple medications to treat their seizures. See <http://www.pharmaceuticalonline.com>. The results of a recent study demonstrate that topiramate has a significant effect on controlling seizures in newly diagnosed epilepsy patients, even when used as a stand-alone therapy. See "New Study Shows TOPAMAX® Used Alone Helps Many Newly-Diagnosed Epilepsy Patients Achieve Seizure Control," <http://www.pharmaceuticalonline.com> (Dec. 11, 2002). Currently, topiramate is approved around the world as adjunctive (add-on) treatment for a variety of seizure types. In addition, more than 30 countries also have approved its use as stand-alone (monotherapy) treatment for epilepsy. In the United States, an application for this use was filed with the Food and Drug Administration in October 2002. If approved, topiramate will be the first AED indicated for initial

Please replace paragraph 0162 with the following paragraph:

Moreover, while topiramate has been shown to be useful in treating obesity, there is a concern that the adverse event profile for the drug will make widespread use of topiramate for treating obesity unlikely. The adverse effect profile in mid-to-late stage clinical trials in obesity included memory problems, fatigue, sleepiness, difficulty in concentration, and tingling in the fingers and toes. As a result of this adverse effect profile, Johnson & Johnson decided to discontinue clinical trials for topiramate for treating obesity. See L. Henderson et al., "J&J will not Pursue Topamax for Obesity," *BTech News* (February 8, 2002) ([www.btechnews.com](http://www.btechnews.com)).

Please replace paragraph 0163 with the following paragraph:

Specifically, a Johnson & Johnson sponsored study recently reported that topiramate, used in combination with an intensive behavioural intervention, seems to be safe and effective for weight reduction in newly diagnosed obese, type 2 diabetics who are following a controlled diet. The study comprised 541 randomized patients who were given 60 weeks treatment with topiramate 96 mg/d or 192 mg/d, or placebo, following a six-week placebo run-in period. However, while positive results were observed, the study was terminated prematurely to develop an improved formulation with the potential for enhanced tolerability in this population. Thus, no patient completed the 52-week maintenance phase. During the study, 19% of patients withdrew because of side effects. The most common treatment-related adverse events were related to the central nervous system and included paraesthesia, fatigue, hypoesthesia, injury, and abnormal vision. The most common adverse events resulting in withdrawal were paraesthesia in 5% of patients, depression in 3%, and difficulty with memory in 3%. See J. Stein, "International Diabetes Federation (IDF): Topiramate Shows Potential for Weight Loss Obese Diabetics" (Aug. 26, 2003); <http://www.docguide.com/news/content.nsf/news/8525697700573E1885256D8E005999FC> (summarizing study results reported on August 25<sup>th</sup> at the Eighteenth International Diabetes Federation (IDF) Congress, entitled "Safety and Efficacy of topiramate in the treatment of type 2 diabetic obese subjects: a randomised, double blind, placebo controlled trial").

Please replace paragraph 0168 with the following paragraph:

In late 2001, the U.S. Department of Energy's Brookhaven National Laboratory reported that topiramate could be a cure for nicotine addiction. *See* "Therapeutic Drug Blocks Nicotine's Effects on Brain Chemistry" (Nov. 8, 2001); <http://www.bnl.gov/bnlweb/pubaf/pr/2001/bnlpr110801.htm>.